

FILE

L15 ANSWER 25 OF 115 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1956:17370 CAPLUS

DN 50:17370

OREF 50:3641i,3642a-b

TI Photosensitization by chlorpromazine

AU Cohen, Irvin M.; Nash, Joe B.

SO Psychiat. Research Repts. (1955), No. 1, 11-13

DT Journal

LA Unavailable

AB Research was undertaken to ascertain whether or not **chlorpromazine** or its one known metabolite, the sulfoxide of **chlorpromazine**, induces photosensitization in humans on **topical** application, or if systemic absorption is required. Aqueous solns. containing 1% chlorpromazine and 1% chlorpromazine sulfoxide were applied to a small area of the skin, allowed to dry, and then exposed to sun lamp radiation. The erythema produced 5-6 hrs. after irradiation in the control area was at least equal to and more frequently was greater than that of the treated site in all patients.

L3 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 1992:639545 CAPLUS  
DN 117:239545  
TI ChronoFilm: a novel transdermal and topical delivery system  
AU Szycher, M.; Tabibi, E.; Siciliano, A.  
CS PolyMedica Ind., Inc., Woburn, MA, 01801, USA  
SO High Perform. Biomater. (1991), 807-12. Editor(s): Szycher, Michael.  
Publisher: Technomic, Lancaster, Pa.  
CODEN: 58DCA6  
DT Conference; General Review  
LA English  
AB A review with 4 refs. on controlled-release self-adhesive delivery systems  
for drugs based on biocompatible polyurethane elastomers (ChromoFilm) for  
transdermal and **topical administration**.

L6 ANSWER 21 OF 405 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1998:608526 CAPLUS  
 DN 129:184644  
 TI Method for reducing coronary artery reactivity using progesterone  
 IN Hermsmeyer, R. Kent  
 PA Dimera, LLC, USA  
 SO PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837897	A1	19980903	WO 1998-US3733	19980226
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 6056972	A	20000502	US 1998-24972	19980206
	AU 9861866	A1	19980918	AU 1998-61866	19980226
PRAI	US 1997-806358	A	19970226		
	US 1998-24972	A	19980206		
	WO 1998-US3733	W	19980226		

AB A method for reducing coronary artery reactivity. A predetd. amount of natural progesterone is provided by a convenient and pleasant delivery system to the blood stream, sufficient to reduce the likelihood of coronary vasospasm and myocardial ischemia. The **progesterone** may be provided either by **topical** application to the epidermis of a cream in which the **progesterone** is dissolved or by patch technol., so as to provide continuous delivery and thereby maintain the level of **progesterone** in the blood stream at least about 1 ng per mL. Kits for dispensing the **topical progesterone** are also claimed. A method is also claimed for screening for compds. that can inhibit coronary vasospasm by testing them in exptl. animals, preferably rhesus monkeys, that have been treated with vasoconstrictive agents that invoke a coronary spasm; the vasoconstrictive agents are preferably serotonin and U46619.

L11 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1998:742241 CAPLUS  
 DN 129:347178  
 TI **Topical** antimicrobial compositions comprising  
**sphingosines** for use in cosmetics  
 IN Lambers, Johannes Wilhelmus Jacobus; Streekstra, Hugo  
 PA Gist-Brocades B.V., Neth.  
 SO PCT Int. Appl., 22 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9849999	A2	19981112	WO 1998-EP2795	19980504
	WO 9849999	A3	19990204		
	W: BR, JP, KR, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 914075	A2	19990512	EP 1998-928252	19980504
	R: DE, ES, FR, GB, IT				
	BR 9804872	A	19990824	BR 1998-4872	19980504
	JP 2000513745	T2	20001017	JP 1998-547751	19980504
	US 6147118	A	20001114	US 1998-214360	19981229
	KR 2000022503	A	20000425	KR 1998-710947	19981231
PRAI	EP 1997-201304	A	19970502		
	WO 1998-EP2795	W	19980504		

AB Topically occurring microbial growth is inhibited by applying a topical composition comprising a sphingoid base. Specifically, said sphingoid base is effectively formulated in combination with a surfactant. Antibacterial activity of sphingosine (I) against *Staphylococcus aureus* and *Corynebacterium xerosis* showed that the amount of colony forming units decreased with an increasing concentration of I from 0.005-0.02%. An anti-acne skin cleansing lotion contained PPG-26 buteth-26 and PEG-40 hydrogenated castor oil 1, phytosphyngosine 0.2, bu

L3 ANSWER 20 OF 160 MEDLINE on STN  
AN 1998010047 MEDLINE  
DN 98010047 PubMed ID: 9349334  
TI The effects of **topical doxepin** on responses to  
histamine, substance P and prostaglandin E2 in human skin.  
AU Sabroe R A; Kennedy C T; Archer C B  
CS University of Bristol, Department of Dermatology, Bristol Royal Infirmary,  
U.K.  
SO BRITISH JOURNAL OF DERMATOLOGY, (1997 Sep) 137 (3) 386-90.  
Journal code: 0004041. ISSN: 0007-0963.  
CY ENGLAND: United Kingdom  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LA English  
FS Priority Journals  
EM 199711  
ED Entered STN: 19971224  
Last Updated on STN: 19971224  
Entered Medline: 19971119  
AB The tricyclic antidepressant, doxepin, is known to have H1 and H2  
antihistaminic effects. Recently, 5% doxepin cream has been marketed in  
the U.S.A. for treatment of eczematous dermatoses. We investigated the  
effects of **topical doxepin** treatment on histamine-,  
substance P- and prostaglandin E2- (PGE2) induced responses in the skin of  
normal and atopic subjects. We compared the effects of **topical**  
**doxepin** with those of the oral antihistamine terfenadine. The  
weal volume and flare area responses to histamine were significantly  
reduced by treatment with **topical doxepin** or oral  
terfenadine in both normal and atopic subjects ( $P < 0.05$ ). The mean +/-  
SEM percentage reduction in flare area for 10 micrograms/site of histamine  
in non-atopics and atopics was 48 +/- 8% and 60 +/- 17% with terfenadine,  
and 54 +/- 12% and 81 +/- 4% with **topical doxepin**,  
respectively. The mean percentage reduction in weal volume for the same  
dose of histamine in non-atopics and atopics was 70 +/- 9% and 63 +/- 16%  
with terfenadine, and 96 +/- 2% and 89 +/- 6% with **topical**  
**doxepin**, respectively. The flare but not the weal response to  
substance P was inhibited by both treatments in all subjects ( $P < 0.05$ ).  
The mean +/- SEM percentage reduction in flare area for 200 pmol/site of  
substance P in non-atopics and atopics was 53 +/- 10% and 73 +/- 4% with  
terfenadine, and 74 +/- 7% and 75 +/- 4% with **topical**  
**doxepin**, respectively. The cutaneous responses to PGE2 were not  
affected by either drug. The inhibitory effects of doxepin were as great  
as those of terfenadine, and doxepin had a significantly greater effect  
than terfenadine in inhibiting the weal response to histamine and flare  
response to substance P in normal volunteers ( $P < 0.05$ ). There was no  
significant difference between atopics and non-atopics in the percentage  
reduction of cutaneous responses by oral terfenadine or **topical**  
**doxepin**. Marked sedation occurred in three of the first 10  
subjects treated with **topical doxepin**, necessitating a  
reduction in dosage for the remaining six subjects. In summary,  
**topical doxepin** was as effective as, and sometimes more  
effective than, a standard dose of oral terfenadine in the inhibition of  
histamine-induced and axon-reflex-mediated cutaneous responses. The  
marked sedative effect may limit its clinical use in some patients.

AUTHOR(S):  
CORPORATE SOURCE:

Hepel, Maria; Mahdavi, Farah  
Department of Chemistry, State University of New York  
at Potsdam, Potsdam, NY, 13676, USA  
Microchemical Journal (1997), 56(1), 54-64  
CODEN: MICJAN; ISSN: 0026-265X

PUBLISHER:

Academic

DOCUMENT TYPE:

Journal

LANGUAGE:

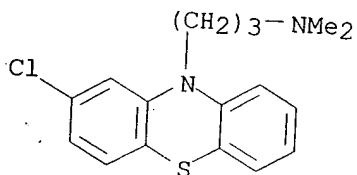
English

AB A new methodol. has been applied to drug release studies. A conductive polymer film was used as a matrix for drug incorporation. The characterization of the polymer films has been obtained by in situ monitoring of the mass change by a quartz crystal microbalance in conjunction with cyclic voltammetry. The electrochem. quartz crystal microbalance (EQCM) with its excellent sensitivity allowed direct measurement of the amt. of the drug released when the potential of the film was changed. New information on ion dynamics under the in situ conditions was obtained. The release of a neuroleptic drug, chlorpromazine (CPZ), from a composite polypyrrole/melanin film upon elec. stimulation has been studied.

IT 50-53-3, Chlorpromazine, biological studies  
RL: PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)  
(application of the electrochem. quartz crystal microbalance for electrochem. controlled binding and release of chlorpromazine from conductive polymer matrix)

RN 50-53-3 CAPLUS

CN 10H-Phenothiazine-10-propanamine, 2-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)



L234 ANSWER 11 OF 45 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1997:144312 CAPLUS  
DOCUMENT NUMBER: 126:190762  
TITLE:

**Melanin** formation inhibitors containing pregnenolones

INVENTOR(S): Hashizume, Ron; Ootsuki, Yoshikazu; Kamoda, Hironobu  
PATENT ASSIGNEE(S): Adobansuto Sukin Risaachi Kenk, Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

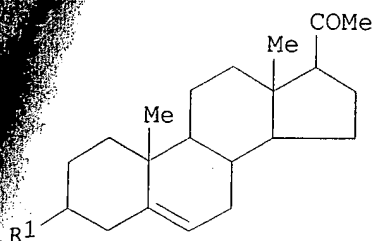
LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08337528	A2	19961224	JP 1995-148623	19950615
OTHER SOURCE(S):		MARPAT 126:190762		
GI				



AB The **melanin** formation inhibitors contain pregnenolones I (R1 = C1-18 carboxyl, OH, OSO<sub>3</sub>H). Pregnenolone (at 25 .mu.M) showed significant whitening effect on cultured HM3KO cells (human skin **melanoma** cells). Formulation examples of ointments, skin lotions, and cosmetic packs are given.

IT 1778-02-5, Pregnenolone acetate 33944-86-4, Pregnenolone palmitate

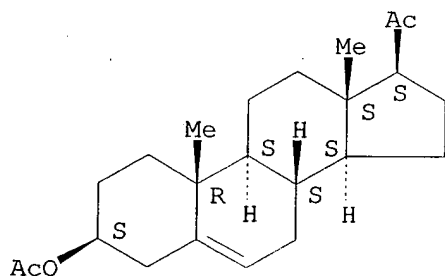
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(pregnenolones as **melanin** formation inhibitors for **skin-lightening**)

RN 1778-02-5 CAPLUS

CN Pregn-5-en-20-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

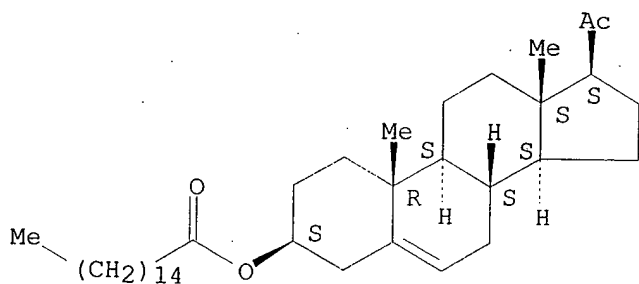
Absolute stereochemistry.



RN 33944-86-4 CAPLUS

CN Pregn-5-en-20-one, 3-[(1-oxohexadecyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L234 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:143747 CAPLUS

Searched by Barb O'Bryen, STIC 308-4291

Page 9  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:

AUTHOR:  
SOURCE:

PUB. COUNTRY:  
DOCUMENT TYPE:  
LANGUAGE:  
FILE SEGMENT:  
ENTRY MONTH:  
ENTRY DATE:

CONTROLLED TERM:

93348096 MEDLINE  
93348096 PubMed ID: 8346126  
Topical progesterone as treatment of choice in genital  
lichen sclerosis et atrophicus in children.  
Serrano G; Millan F; Fortea J M; Grau M; Aliaga A  
PEDIATRIC DERMATOLOGY, (1993 Jun) 10 (2) 201.  
Journal code: 8406799. ISSN: 0736-8046.  
United States  
Letter  
English  
Priority Journals  
199309  
Entered STN: 19930924  
Last Updated on STN: 19930924  
Entered Medline: 19930909  
Check Tags: Female; Human; Male  
Administration, Cutaneous  
Child  
Chronic Disease  
\*Genital Diseases, Female: DT, drug therapy  
\*Genital Diseases, Male: DT, drug therapy  
\*Lichenoid Eruptions: DT, drug therapy  
\*Pigmentation Disorders: DT, drug therapy  
\*Progesterone: TU, therapeutic use  
57-83-0 (Progesterone)

CAS REGISTRY NO.:

L234 ANSWER 31 OF 45  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:

AUTHOR:  
SOURCE:

PUB. COUNTRY:  
DOCUMENT TYPE:  
LANGUAGE:  
FILE SEGMENT:  
ENTRY MONTH:  
ENTRY DATE:

CONTROLLED TERM:

89379530 MEDLINE  
89379530 PubMed ID: 2777449  
The use of readily available photosensitizers for vitiligo  
in Nigeria.  
George A O  
INTERNATIONAL JOURNAL OF DERMATOLOGY, (1989 Sep) 28 (7)  
475-7.  
Journal code: 0243704. ISSN: 0011-9059.  
United States  
Letter  
English  
Priority Journals  
198910  
Entered STN: 19900309  
Last Updated on STN: 19900309  
Entered Medline: 19891020  
Check Tags: Case Report; Female; Human  
Adult  
Child, Preschool  
\*Chlorpromazine: TU, therapeutic use  
Nigeria  
\*Promethazine: TU, therapeutic use  
Soaps  
\*Sunlight  
\*Vitiligo: DT, drug therapy  
50-53-3 (Chlorpromazine); 60-87-7 (Promethazine)  
0 (Soaps)

CAS REGISTRY NO.:  
CHEMICAL NAME:

L234 ANSWER 32 OF 45  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:  
AUTHOR:

CORPORATE SOURCE:

88339384 MEDLINE  
88339384 PubMed ID: 2844124  
Microprobe analysis of chlorpromazine pigmentation.  
Benning T L; McCormack K M; Ingram P; Kaplan D L; Shelburne  
J D  
Department of Pathology, Duke University Medical Center,  
Durham, NC 27710.

Searched by Barb O'Bryen, STIC 308-4291



cleared after chlorpromazine was discontinued. They suggest that loxapine may be a suitable alternative to phenothiazines when skin pigmentation and ocular involvement occur, although the patient must be carefully monitored for ocular problems.

CONTROLLED TERM: Check Tags: Case Report; Human; Male  
\*Chlorpromazine: AE, adverse effects  
Chlorpromazine: TU, therapeutic use  
Chronic Disease  
\*Dibenzoxazepines: TU, therapeutic use  
\*Eye Color: DE, drug effects  
\*Loxapine: TU, therapeutic use  
Middle Age  
Photosensitivity Disorders: CI, chemically induced  
\*Schizophrenia: DT, drug therapy  
\*Skin Pigmentation: DE, drug effects  
CAS REGISTRY NO.: 1977-10-2 (Loxapine); 50-53-3 (Chlorpromazine)  
CHEMICAL NAME: 0 (Dibenzoxazepines)

L234 ANSWER 36 OF 45 MEDLINE  
ACCESSION NUMBER: 67014260 MEDLINE  
DOCUMENT NUMBER: 67014260 PubMed ID: 5917622  
TITLE: Therapy of Phenothiazine-produced skin pigmentation: a preliminary report.  
THOR: Gibbard B A; Lehmann H E  
URCE: AMERICAN JOURNAL OF PSYCHIATRY, (1966 Sep) 123 (3) 351-2.  
Journal code: 0370512. ISSN: 0002-953X.  
JB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
ILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
NTRY MONTH: 196612  
NTRY DATE: Entered STN: 19900101  
Last Updated on STN: 19900101  
Entered Medline: 19661226  
CONTROLLED TERM: Check Tags: Female; Human  
\*Ascorbic Acid: TU, therapeutic use  
\*Chlorpromazine: AE, adverse effects  
\*Penicillamine: TU, therapeutic use  
\*Pigmentation Disorders: CI, chemically induced  
\*Pigmentation Disorders: DT, drug therapy  
Schizophrenia: DT, drug therapy  
CAS REGISTRY NO.: 50-53-3 (Chlorpromazine); 50-81-7 (Ascorbic Acid); 52-67-5 (Penicillamine)

L234 ANSWER 37 OF 45 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-340107 [37] WPIDS  
DOC. NO. NON-CPI: N2002-267371  
DOC. NO. CPI: C2002-097809  
TITLE: Human lung-originated G protein-coupled receptor protein TGR19 and encoded DNA, for developing drugs to treat diseases of central nervous system, and circulatory system, inflammatory diseases and cancer.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): ITO, T; MIWA, M; MIYAJIMA, N; SHINTANI, Y  
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD  
COUNTRY COUNT: 96  
PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

COUNTRY: United States  
DOCUMENT TYPE: Journal Article  
FILE SEGMENT: 016 Cancer  
037 Drug Literature Index

~~FILE~~

LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Tamoxifen has been reported to have numerous physiological effects that are independent of the estrogen receptor, including sensitization of resistant tumor cells to many chemotherapeutic agents. Drug-resistant cells sequester weak base chemotherapeutics in acidic organelles away from their sites of action in the cytosol and nucleus. This work reports that tamoxifen causes redistribution of weak base chemotherapeutics from acidic organelles to the nucleus in drug-resistant cells. Agents that disrupt organelle acidification (e.g., monensin, bafilomycin A1) cause a similar redistribution. Measurement of cellular pH in several cell lines reveals that tamoxifen inhibits acidification of **endosomes** and **lysosomes** without affecting cytoplasmic pH. Similar to monensin, tamoxifen decreased the rate of vesicular transport though the recycling and secretory pathways. Organellar acidification is required for many cellular functions, and its disruption could account for many of the side effects of tamoxifen.

L84 ANSWER 22 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1998386460 EMBASE  
TITLE: Effect of bafilomycin A1 and nocodazole on endocytic transport in HeLa cells: Implications for viral uncoating and infection.

AUTHOR: Bayer N.; Schober D.; Prchla E.; Murphy R.F.; Blaas D.; Fuchs R.

CORPORATE SOURCE: R. Fuchs, General/Experimental Pathology Dept., University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria. reate.fuchs@akh-wien.ac.at

SOURCE: Journal of Virology, (1998) 72/12 (9645-9655).  
Refs: 74

ISSN: 0022-538X CODEN: JOVIAM  
United States

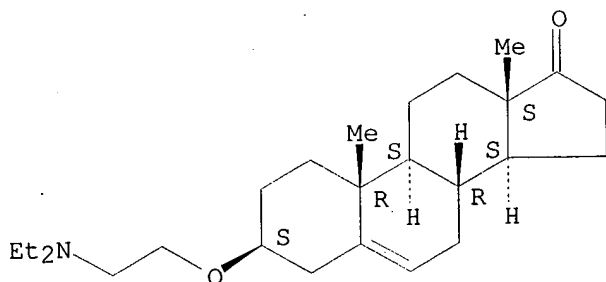
COUNTRY:

DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Bafilomycin A1 (baf), a specific inhibitor of vacuolar proton ATPases, is commonly employed to demonstrate the requirement of low endosomal pH for viral uncoating. However, in certain cell types baf also affects the transport of endocytosed material from early to late endocytic compartments. To characterize the endocytic route in HeLa cells that are frequently used to study early events in viral infection, we used 35S-labeled human rhinovirus serotype 2 (HRV2) together with various fluid-phase markers. These virions are taken up via receptor-mediated endocytosis and undergo a conformational change to C-antigenic particles at a pH of <5.6, resulting in release of the genomic RNA and ultimately in infection (E. Prchla, E. Kuechler, D. Blaas, and R. Fuchs, J. Virol. 68:3713-3723, 1994). As revealed by fluorescence microscopy and subcellular fractionation of microsomes by free-flow electrophoresis (FFE), baf arrests the transport of all markers in early endosomes. In contrast, the microtubule-disrupting agent nocodazole was found to inhibit transport by accumulating marker in endosomal carrier vesicles (ECV), a compartment intermediate between early and late **endosomes**. Accordingly, **lysosomal** degradation of HRV2 was suppressed, whereas its conformational change and infectivity remained unaffected by this drug. Analysis of the subcellular distribution of HRV2 and fluid-phase markers in the presence of nocodazole by FFE revealed no difference from the control incubation in the absence of nocodazole. ECV and late endosomes thus have identical electrophoretic mobilities, and intraluminal pHs of <5.6 and allow uncoating of HRV2. As bafilomycin not only dissipates the low endosomal pH but also blocks transport from early to late endosomes in HeLa cells, its inhibitory effect on viral infection could in part also be attributed to trapping of virus in early endosomes which might lack components essential for uncoating. Consequently, inhibition of viral uncoating by bafilomycin cannot be taken to indicate a low pH requirement only.

Androst-5-en-17-one, 3-[2-(diethylamino)ethoxy]-, hydrochloride,  
(3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:150925 CAPLUS

DOCUMENT NUMBER: 130:295103

TITLE: Localization of Niemann-Pick C1 protein in astrocytes: implications for neuronal degeneration in Niemann-Pick type C disease

AUTHOR(S): Patel, Shutish C.; Suresh, Sundar; Kumar, Ujendra; Hu, C. Y.; Cooney, Adele; Blanchette-Mackie, E. Joan; Neufeld, Edward B.; Patel, Ramesh C.; Brady, Roscoe O.; Patel, Yogesh C.; Pentchev, Peter G.; Ong, Wei-Yi  
CORPORATE SOURCE: Neurobiology Research Laboratory, Veterans Affairs Connecticut Healthcare System, Newington, CT, 06111, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(4), 1657-1662  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Niemann-Pick type C disease (NP-C) is an inherited neurovisceral lipid storage disorder characterized by progressive neurodegeneration. Most cases of NP-C result from inactivating mutations of NPC1, a recently identified member of a family of genes encoding membrane-bound proteins contg. putative sterol sensing domains. By using a specific antipeptide antibody to human NPC1, the authors have here investigated the cellular and subcellular localization and regulation of NPC1. By light and electron microscopic immunocytochem. of monkey brain, NPC1 was expressed predominantly in perisynaptic astrocytic glial processes. At a subcellular level, NPC1 localized to vesicles with the morphol. characteristics of **lysosomes** and to sites near the plasma membrane. Anal. of the temporal and spatial pattern of neurodegeneration in the NP-C mouse, a spontaneous mutant model of human NP-C, by amino-cupric-silver staining, showed that the terminal fields of axons and dendrites are the earliest sites of degeneration that occur well before the appearance of a neurol. phenotype. Western blots of cultured human fibroblasts and monkey brain homogenates revealed NPC1 as a 165-kDa protein. NPC1 levels in cultured fibroblasts were unchanged by incubation with low d. lipoproteins or oxysterols but were increased 2- to 3-fold by the drugs progesterone and U-18666A, which block cholesterol transport out

of **lysosomes**, and by the **lysosomotropic** agent  $\text{NH}_4\text{Cl}$ .

These studies show that NPC1 in brain is predominantly a glial protein present in astrocytic processes closely associated with nerve terminals, the earliest site of degeneration in NP-C. Given the vesicular localization of NPC1 and its proposed role in mediating retroendocytic trafficking of cholesterol and other **lysosomal** cargo, these results suggest that disruption of NPC1-mediated vesicular trafficking in astrocytes may be linked to neuronal degeneration in NP-C.

IT 3039-71-2, U-18666A

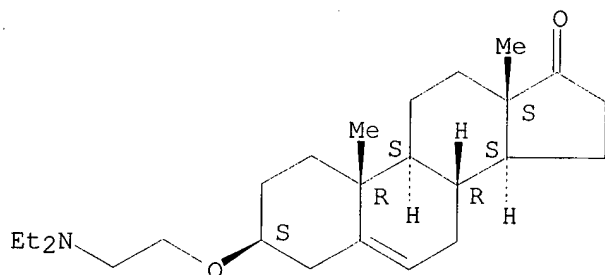
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(Niemann-Pick C1 protein in fibroblasts of humans response to cholesterol transport-blockers progesterone and U-18666A and **lysosomotropic**  $\text{NH}_4\text{Cl}$ )

RN 3039-71-2 CAPLUS

CN Androst-5-en-17-one, 3-[2-(diethylamino)ethoxy]-, hydrochloride, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:105930 CAPLUS

DOCUMENT NUMBER: 130.279626

TITLE: U18666A inhibits intracellular cholesterol transport and neurotransmitter release in human neuroblastoma cells

AUTHOR(S): Sparrow, Susan M.; Carter, Jodi M.; Ridgway, Neale D.; Cook, Harold W.; Byers, David M.

CORPORATE SOURCE: Atlantic Research Centre, Departments of Pediatrics and Biochemistry, Dalhousie University, Halifax, NS, B3H 4H7, Can.

SOURCE: Neurochemical Research (1999), 24(1), 69-77

CODEN: NEREDZ; ISSN: 0364-3190

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To det. if neurochem. function might be impaired in cell models with altered cholesterol balance, we studied the effects of U18666A (3-.beta.-[(2-diethyl-amino)ethoxy]androst-5-en-17-one) on intracellular cholesterol metab. in three human neuroblastoma cell lines (SK-N-SH, SK-N-MC, and SH-SY5Y). U18666A (.ltoreq.0.2 .mu.g/mL) completely inhibited low d. lipoprotein (LDL)-stimulated cholesterol esterification in SK-N-SH cells, while cholesterol esterification stimulated by